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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/558,232	04/26/2000	David M. Manyak	06695.0003	9717

22852 7590 05/19/2004

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/558,232	MANYAK ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56,58-105,107,108,110-129 and 132-142* is/are pending in the application.

4a) Of the above claim(s) *4-9,11-13,24-26,29-32,58,65,66,69 and 111-119* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *88 and 95* is/are objected to.

8)☒ Claim(s) *1-56,58-105,107,108,110-129 and 132-142* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *January 15, 2004* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 1-3,10,14-23,27,28,33-56,59-64,67,68,70-87,89-94,96-105,107,108,110,120-129 and 132-142.

DETAILED ACTION

1. Applicants' arguments filed April 05, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

3. The amendment, filed April 05, 2004, has been entered.

4. Applicant's summary of the February 03, 2004 interview has been accepted.

5. Applicant has failed to summarize the interview of January 15, 2004, as required. It is required that Applicant includes a summary of the interview of January 15, 2004 in the reply to the instant Office Action.

6. The cancellation of claims 57, 106, 109, 130, and 131 has been acknowledged.

7. The withdrawal of claims 4-9, 11-13, 24-26, 29-32, 58, 65, 66, 69, and 111-119 has been acknowledged.

8. The addition of new claims 139-142 has been acknowledged.

9. Claims 1-3, 10, 14-23, 27, 28, 33-56, 59-64, 67, 68, 70-105, 107, 108, 110, 120-129, and 132-142, a system comprising a memory of data about compounds and targets with interaction information, known compounds with known biological activity, have failed in pre-clinical or human clinical test, and molecular targets which include receptors, are examined on the merits.

10. NON-FINAL OFFICE ACTION.

OBJECTIONS

11. Claims 88 and 95 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The amendment to the specification, filed September 10, 2003, is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 5, item n), and page 6, item o). It is acknowledged that Applicant has proposed an amendment to the specification by removing "http://"; such amendment does not inactivate the above cited hyperlinks. Applicant(s) is/are required to delete the embedded hyperlink and/or other form of browser-executable code, or inactivate the hyperlink. See MPEP § 608.01.

NEW MATTER TO THE SPECIFICATION

13. The amendment filed September 10, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

14. The attempt to incorporate subject matter in the amendment, filed September 10, 2003, (Figures 1C, 1D, 2A, 3A, 7A, 7B, 7C, 8A, and 8B, pages 16, 17, 19, 20, 22, 23, 26, 29, and 33) into this application by reference to Provisional Application No. 60/130,992 is improper. Provisional Application No. 60/130,992 is not supported by the instant specification (pages 13-15) as originally filed as a document that has been incorporated by reference. No where in the instant application does the specification recite the statement that Provisional Application No. 60/130,992 is "hereby incorporated by reference." Further, Applicant asserts that Applicant has claimed priority to said Provisional Application No. 60/130,992 in the instant specification (See page 303 of the response filed September 10, 2003). It is noted that the instant specification claims priority to Provisional Application No. 60/008,660 as indicated by page 2 of the instant specification as originally filed. The proposed subject matter to be incorporated has not been found in the priority document Provisional Application No. 60/008,660.

15. Applicant is required to cancel the new matter in the reply to this Office Action.

CLAIM REJECTIONS - 35 USC § 101

16. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

17. Claims 37, 41-49, 52-56, and 133-138 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory algorithm type subject matter.

18. Claims 37, 41-49, 52-56, and 133-138 are rejected because said claims are directed to a computer system, memory for storing data, and database, comprising steps for correlating data without any physical alteration step, which is considered to be non-statutory subject matter. "For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory." (MPEP § 2106 (IV)(B)(2) (b), part ii). Similar to the nonstatutory example above, the instant invention comprises algorithmic steps for correlating data without any physical alteration resulted from said analysis steps. Further, the instant invention is directed to steps for correlating data without any physical alteration of said data outside of said computer system, memory for storing data, or database.

CLAIM REJECTIONS - 35 USC § 112, FIRST PARAGRAPH

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 44, 46, 47, 54-56, 60, 61, 63, 64, 67, 68, 77, 78, 87, 89, 96, 102, 108, 110, and 132-141 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

21. THIS IS A NEW MATTER REJECTION.

22. This rejection is maintained with respect to claims 67, 68, 77, 78, 87, 89, 96, 102, and 108, as recited in the previous office action mailed March 10, 2003, and claim 110, as recited

in the previous action mailed December 04, 2003. The instant rejection has been extended to claims 44, 46, 47, 54-56, 60, 61, 63, 64, and 132-141.

23. Applicants argue to overcome said rejection by amending said claims to recite limitations that have been disclosed in the Provisional Application (60/130,992), which has been asserted by Applicant to be incorporated by reference. Applicants' argument has been fully considered and found to be unpersuasive due to the subject matter being submitted in the said amendment has been determined to be improper as discussed above.

24. The limitations of "new information reflecting a relationship", claim 44, line 8, "new relationship", claim 46, line 11, "a process identifies a new relationship...in the second database", claim 139, lines 17-18, and "new relationship", claims 140 and 141, line 1, have not been found in the instant specification. Therefore, said limitation has been considered to be new matter. It is noted that there is disclosure for a process of identifying "new drug candidates" throughout the instant specification. However, the disclosure of a process of identifying "new drug candidates" does not support the limitation of "new information reflecting a relationship" or "a process identifies a new relationship" as recited in claim 44 or 139. Claim 47 is rejected for being dependent from claim 46.

25. Specific to claim 54, the limitation of "creating a full-rank data set of test results" has not been found in the instant specification. It is noted that the instant specification discloses "a full-rank screening database" (page 9, lines 7-9) which is different from the limitation of "a full-rank data set of test results." The limited disclosure of the specification does not support

the general limitation of the claims. Claims 55 and 56 are rejected for being dependent from claim 54.

26. Specific to claim 54, line 5, and claim 132, line 9, the limitation of "all possible combinations of the compounds selected" has not been found in the instant specification. Specific to claims 60 and 63, lines 3-4, the limitation of "interaction between all of the compounds...and all or substantially all of the molecular targets" has not been found in the instant specification. Specific to claim 137, lines 3-5, the limitation of "interaction between all or substantially all... and all or substantially all of a plurality of molecular targets" has not been found in the instant specification. Therefore, said limitations have been considered to be new matter. Claims 55 and 56 are rejected for being dependent from claim 54. It is acknowledged that claims 60, 63, and 137 are indicated as being previously presented. However, these claims have been newly added in the claim amendment, filed October 29, 2002, after the filing date of the instant application.

27. Specific to claims 61 and 64, line 3, the limitation of "a majority of the compounds" has not been found in the instant specification. Specific to claim 138, line 3, the limitation of "a majority of a plurality of compounds" has not been found in the instant specification. Therefore, said limitations have been considered to be new matter. It is acknowledged that claims 61, 64, and 138 are indicated as being previously presented. However, these claims have been newly added in the claim amendment, filed October 29, 2002, after the filing date of the instant application.

28. Specific to claim 133, lines 6-7, the limitation of "identified chemical compounds" or "identified molecular targets" has not been found in the instant specification. Therefore, said limitation has been considered to be new matter. Claims 134-138 are rejected for being dependent from claim 133.

CLAIM REJECTIONS - 35 USC § 103

29. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

30. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

31. Claims 1-3, 14-23, 27, 28, 33-56, 59-64, 70-76, 78, 80, 89-91, 93, 94, 97-105, 120, 121, 124, 125, 127-129, and 132-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goto et al. (1998) taken with Bult et al. (May 1999) in combination with Antman et al. (1992).

RESPONSE TO APPLICANT'S ARGUMENT

32. Specific to independent claims 1, 33, 35, 37, 44, 45, 54, 59, and 132, Applicant argues that Goto et al. does not disclose at least a third database containing records corresponding to tests of interactions between compounds in the first database and molecular targets in the second databases. Further, Applicant argues that Goto et al. does not store "screening results from tests of interactions between each of a plurality of compounds in a first database and each of a plurality of molecular targets in a second database."

33. Applicant's argument has been fully considered and found to be unpersuasive as discussed below.

34. Specific to the argument that Goto et al. does not disclose the limitation of "compound interacts with each of the many molecular targets database (e.g. a one to many relationship)", Goto et al. discloses KEGG (third database) which generates pathway diagrams (records) via LIGAND and makes the connection of two neighboring enzymes (one-to-many) (second database) on the metabolic pathway which is the result of the common compound that is both the product of the first reaction and the substrate of the second reaction. The network of enzymes can be computed by generating networks of chemical compounds from a set of substrate-product relationships (biological information related to effects on a biological system). It is possible to generate all possible paths for all compounds (first database) (page 596, columns 1-2, Path computation of LIGAND §).

35. KEGG as a computerized database of mechanisms of gene functions and cellular functions in terms of the information pathways that consist of interacting genes or molecules (Page 591, Column 1, Lines 23-26). LIGAND is accessible through the KEGG systems

(processor) via the Japanese GenomeNet database (storage memory) and the LIGAND database is downloadable (page 591, column 1, Availability §).

36. COMPOUND (first database) comprises all chemical compounds identified by accession numbers that appear in ENZYME such as substrates, products, inhibitors, cofactors, and effectors with their respective reaction data (effect) (page 593, column 2, COMPOUND section). Goto et al. include compounds from living cells (biological systems) and all compounds that are related (effect) to known metabolic pathways into the COMPOUND database (page 595, column 1, lines 1-9), as instant claim 1, lines 1-4; claim 33, lines 1-3; claim 35, lines 1-4; claim 37, lines 1-4; claim 44, lines 1-3; claim 54, lines 1-4; claim 46, lines 1-3; claim 59, lines 1-3; and claim 132, lines 1-3.

37. Goto et al. discloses ENZYME (second database) comprising the description of enzymes identified by EC numbers (molecular targets) and the reactions it catalyzes, and the collection of chemical compounds that are related to the enzyme (page 592, column 2, ENZYME section), as in instant claim 1, lines 5-6; claim 33, lines 1-3; claim 35, lines 5-6; claim 37, lines 5-6; claim 44, lines 4; claim 45, lines 5-6; claim 46, lines 5-6; claim 49, claim 59, lines 4-5; and claim 132, lines 4-5.

38. Goto et al. discloses KEGG pathway database (third databases) (Figure 3) wherein KEGG makes "connections between the factual data for individual molecules, i.e., gene and gene products, and the biological relationships among them, i.e. molecular interactions and molecular pathways" (page 595-596, Pathway reconstruction with LIGAND §). KEGG (third database) generates pathway diagrams (records) via LIGAND and makes the

connection of two neighboring enzymes (second database) on the metabolic pathway which is the result of the common compound that is both the product of the first reaction and the substrate of the second reaction. The network of enzymes (second database) can be computed by generating networks of chemical compounds from a set of substrate-product relationships (biological information related to effects on a biological system). It is possible to generate all possible paths for all compounds (first database) (page 596, columns 1-2, Path computation of LIGAND §). Goto et al. identifies new chemical compounds (screen results) appearing in these reactions and add them as new COMPOUND entries. "The reactions and compounds (screening results) are also stored in the relational database for the main purpose of pathway computation (page 597, column 1, Organization of LIGAND §) via KEGG (third database), as in instant claim 1, lines 7-13; claim 33, lines 6-12; claim 35, lines 7-9; claim 37, lines 7-13; claim 44, lines 5-6; claim 45, lines 7-8 and 11-15; claim 46, lines 7-10; claim 54; claim 59, lines 6-8; claim 60; claim 61; claim 132, lines 6-12; and claim 133.

39. KEGG (third database) via LIGAND is intended to give all possibilities, from which the user can maker further reasoning (new information) based on the parameter constraints (threshold) (page 597, column 2, lines 6-13), as in instant claim 23; claim 44, lines 7-10; claim 46, lines 11-12; claim 137; and 138.

40. The results are in a Webpage (user interface) comprising chemical structure as directed to the enzyme (second database) and compounds (first database) (page 598, column 1, lines 3-9, and figures 1-2), as in instant claim 1, lines 14-17; claim 33, lines 13-16; claim 35, lines 10-

13; claim 38; claim 39; claim 40; claim 51; claim 52; claim 59, lines 9-12; claim 63; claim 64; and claim 132, lines 13-16.

41. Figure 2 illustrates a data set of results comprising rank order of EC numbers of enzymes associated with the specified compounds, as in instant claim 54, line 7.

42. Enzyme entry contains links to GENES database (fourth database) and DISEASE fields describes human genetic disorders as directed to enzymes, which is linked to OMIM database (fourth database) (page 593, column 1, lines 1-19), as in claim 45, lines 9-10; and claim 62.

43. Goto et al. teaches "new activities of computational functional genomics that include the identification of biological functions of unknown gene products,...comparative analysis of genes and genomes in different species, and analysis and simulation of gene expressions in different cells or in different developmental stages. In order to facilitate such post-genomic sequencing analyses, it has become a high priority to construct a new breed of database that defines functional aspects of genes, cells and organisms" (Page 591, Column 2, Lines 12-22), as in instant claims 78, 128, and 129.

44. The sequence data is captured from recent progress in genome sequencing from bacteria to eukaryotes (screening process) as directed to biological functions (page 591, column 2, lines 9-22), as in instant claims 70 and 76.

45. "A schematic diagram showing LIGAND as an interface of KEGG (Kyoto Encyclopedia of Genes and Genomes) and DBGET/LinkDB systems as well as an interface of biological

and chemical databases" (Figure 3, page 596). LIGAND comprises data directed to PIR superfamily (page 597, column 1, lines 11-14), as in instant claim 124.

46. KEGG makes connections between the factual data for individual molecules, i.e. genes and gene products, and the biological relationships among them, i.e. molecular interactions and molecular pathways" (Page 595, Column 2, Lines 1-2 and Page 596, Column 1, Lines 1-4), as in instant claims 104 and 127.

47. The KEGG project includes databases such as PATHWAY, COMPOUND, GENES and interaction databases such as ENZYME for enzymatic reactions and BRITE for molecular interactions in general. Specific to the BRITE database, molecular interactions may include those determined from the yeast two-hybrid system for protein-protein interaction (binding) (Page 597, Lines 32-46). Table 3 illustrates records from KEGGS corresponding to enzyme (molecular targets) group by species source (page 595), as in instant claims 3, 27, 41, 42, 103, 125, and 135.

48. "LIGAND now consists of two sections: the expanded ENZYME section and the new COMPOUND section...The COMPOUND section is a collection of metabolic compounds, including substrates, products, inhibitors, cofactors and effectors, and other chemical compounds that play important functional roles in living cells" (Page 592, Column 1, Lines 49-53), as in instant claim 2.

49. "Each compound is given an accession number in the ENTRY field, which is followed by the compound name and its synonyms in the NAME field, and the molecular formula in

the FORMULA field." The DBLINKS field includes the CAS registry (Page 593, Column 2, Lines 10-28), as instant claims 14, 15, and 18-22.

50. Tables 1 and 2 disclose the number of links from ENZYME to other databases where users can view information for enzymes whose roles in the metabolic pathways are known and whose sequences and three-dimensional structures have been determined (Page 594, Column 2, Lines 13-17), as in instant claims 97, 98, and 120.

51. The number of entries such as inhibitors or effectors (known biological activity) and links in COMPOUND are disclosed in Table 4 (Page 595), as in instant claims 28, 34, 36, 42, 43, 47, 48, 99, and 134.

52. "The LIGAND database thus provides fundamental data on both biological and chemical aspects of life" (Page 592, Column 2, Lines 4-5). "The DISEASE field describes human genetic disorders caused by a lack of or mutation of the enzyme, which is linked to the OMIM database. The MOTIF field describes the protein sequence motifs that are linked to PROSITE...and the STRUCTURE field contains the code names of the protein three-dimensional structures in the Protein Data Bank" (Page 593, Column 1, Lines 11-19). "The chemical structure is entered in our database in the MDL MOL file format, which can also be downloaded in DBGET/LinkDB to launch a helper application, such as ISIS/Draw, to view and manipulate the structure (related methods), as in instant claims 89-91, 93, and 94.

53. The COMPOUND section is constructed manually, except for the link information to ENZYME and KEGG/PATHWAY, by consulting with various sources, such as the Merck

Index (Budavari, 1996), and dictionaries of biochemistry and organic chemistry" (Page 593, Column 2, lines 28-32).

54. The inclusion of a document containing the description of the Merck Index is provided to support and expand on prior art cited from Goto et al. The Merck Index has the following type of information available: biological products, environmentally significant compounds, and natural products. "The MERCK INDEX ONLINE is made available through major online database vendors" (Page V, Lines 13-15 and 31-32), as in instant claim 16.

55. Specifically, the drug information disclosed in the Merck Index include the following: compound name, compound type, references to pharmacological or biological activity, clinical trials, toxicity studies, structure, and physical data which includes solubilities determined at room temperature, therapeutic category, metabolism in humans (Page ix and Page x, Lines 17-19, Structure section, Physical Data section, and Literature References section), as in instant claims 53, 100-102, 140, and 141.

56. "LIGAND database provides the enzyme classification according to EC number...For instance, the sequence similarity can be used to define a hierarchical classification of families and superfamilies of functionally related proteins...The sequence and structural motifs that have been extracted from groups of enzymes with similar functions can also be considered as a functional hierarchy" (Page 596, Lines 24-26 and 30-33), as in instant claims 105 and 121.

57. Further, LinkDB provide access to ATPase EC 3.6.1.3, which is further linked to literature source via the ENZYME nomenclature database (ExPASy) that provide disclosure for ATPase in regard to binding and inhibition assays. A document by Liu et al. (1997) is

provided not as prior art but only as disclosure to the data that is accessible via LinkDB. From LinkDB, EC 3.6.1.3 provides a link to reference literature via ExPASy specific to ATPase. For example, Liu et al. discloses "the assay uses Mg2+ ions to permeabilize membrane vesicles or proteoliposomes, thus allowing access of ATP to both sides of the bilayer. HisQMP2 displays a low level of intrinsic ATPase activity in the absence of HisJ; unliganded HisJ stimulates the activity and liganded HisJ stimulates to an even higher level. All three levels of activity display positive cooperativity for ATP with a Hill coefficient of 2 and a K0.5 value of 0.6 mM. The activity has been characterized with respect to pH, salt, phospholipids, substrate, and inhibitor specificity. Free histidine has no effect" (Abstract). "Vanadate, a potent inhibitor of P-type ATPases and histidine transport, inhibits the activity of HisQMP2, giving 50% inhibition (potency) at 6.5 μM. Bafilomycin A1 (100 μM), oubain (up to 3 mM), and NaN3 (10 mM) do not inhibit" (Page 21887, column 2, lines 23-28), as in instant claims 55, 56, 71-75, 80, and 136.

58. However, Goto et al. (1998) does not disclose the limitation of a first database of chemical compounds that have failed in preclinical or human clinical tests, as in instant claims 17 and 142, and as an option of the elected subject matter species.

59. Bult et al. discloses a general method for accessing resources and databases available on the World Wide Web that are pertinent to cancer research. It is noted the primary focus of Bult et al. is not on clinical trial information (page 397, column 1, lines 1-7). However, the clinical type of databases (page 406, column 1, Pathology §, to page 407, column 2, Cancer Biology Results Sites), nucleotide and protein databases (page 405, column 2, lines 13-22),

and the suggested uses of said databases disclosed by Bult et al. would have motivated one of ordinary skill in the art at the time of the instant invention to use a World Wide Web resource such as KEGG for nucleotide and protein data with the clinical database directed to compounds of Antman et al. as discussed below.

60. Antman et al. discloses an improvement for "better databases" for the treatment of patients in clinical trials (page 240, Conclusions §). The database of Antman et al. comprises data directed to treatments that have no effect on mortality or are potentially harmful (page 240, Data Synthesis §) and "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) (page 246, column 1, "Negative" RCTs §). The database of Antman et al. comprises information directed to treatment therapies using a plurality of drugs (compounds) and their effects on patients (biological systems) (page 241, column 3, lines 3 to last line), as in instant claims 17 and 142.

61. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Bult et al. for accessing resources directed to clinical type of data, and nucleotide and protein databases via the World Wide Web to access KEGG data directed to nucleotide and protein sequences, compounds, and human genetic disorders (page 593, column 1, lines 11-14) of Goto et al. One of ordinary skill in the art would have been motivated to build "better databases" by integrating the COMPOUND database (first database) of KEGG with data from drug treatments (compounds) failed in human clinical tests as disclosed by Antman et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the instant invention was made to use

KEGG wherein the COMPOUND database (first database) is directed to data from compounds failed in human clinical tests as disclosed by Goto et al., Bult et al., and Antman et al.

62. Claims 1, 10, 17, 59, 67, 68, 79, 81-86, 92, 108, 122, and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogata et al. (1999) taken with Bult et al. (May 1999) in combination with Antman et al. (1992).

RESPONSE TO ARGUMENTS

63. Specific to claims 1 and 59 Applicant argues that for the same reason as Goto et al., Ogata et al. does not disclose at least a third database containing records corresponding to tests of interactions between compounds in the first database and molecular targets in the second databases. Applicant's argument has been fully considered and found to be unpersuasive as discussed below.

64. It is re-iterated Ogata et al. discloses KEGG is tightly integrated with the LIGAND chemical database for enzyme reactions as well as with most of the major molecular biology databases by the DBGET/LinkDB system" (Page 29, Column 2, Lines 1-6).

65. The inclusion of citations from Goto et al. is not being used as prior art, but only to expand on the capabilities of LIGAND, which is disclosed by Ogata et al. The disclosure of Goto et al. discussed above (paragraphs 33-39) anticipates the limitations of claims 1 and 59 as directed to the first, second, and third database comprising interaction data between compounds and molecular targets.

66. Ogata et al. discloses "co-linearity of genes between two genomes is quite useful for identification of clusters of orthologous genes. KEGG provides the comparative genome map for identification of such clusters and for functional annotation of newly sequenced genomes (Page 33, Column 1, Lines 33 and Figure 3). Table 3 shows the list of currently available tools such as gene cluster search and sequence similarity search for search and analysis of KEGG pathway maps and genome maps (Page 33, Column 2, Lines 54-55), as in instant claims 122 and 123.

67. The KEGG biochemical pathways include Ligand-Receptor Interaction (Page 30, Table 2, Cell Processes) as in instant claims 10, 67, 68, and 108.

68. "Thus, it is easy to see how the information of gene expression profiles can be used as still another constraint against the KEGG reference pathway maps. In fact, KEGG provides a tool to color the pathway maps in order to visualize, for example, the microarray patterns of gene expression profiles" (Page 33, Column 2, Lines 48-53). It is inherent in such techniques as the yeast two-hybrid system (page 34, column 1, lines 32-37) and microarray expression assays that interactions are determined by some potency value or compared to some specified threshold value, as in instant claims 79 and 81-86.

69. The inclusion of a document by Schena et al. is not being used as prior art but only to show the inherent properties of microarray expression arrays as cited above. Schena et al. dislcoses microarray expression data consists of ratio measurements and differential expression is derived from determining the order of magnitude changes for the intensity values wherein the potency of interaction is determined for the ratios greater a specified threshold (Schena et al., page 10615, column 2, lines 5-14).

70. Further, the process of generating gene clusters or gene expression profiles is a type of recursive partitioning, as in instant claim 92.

71. However, Ogata et al. does not disclose the limitation of a first database of chemical compounds that have failed in preclinical or human clinical tests, as in instant claim 17, and as an option of elected subject matter species.

72. Bult et al. discloses a general method for accessing resources and databases available on the World Wide Web that are pertinent to cancer research. It is noted the primary focus of Bult et al. is not on clinical trial information (page 397, column 1, lines 1-7). However, the clinical type of databases (page 406, column 1, Pathology §, to page 407, column 2, Cancer Biology Results Sites), nucleotide and protein databases (page 405, column 2, lines 13-22), and the suggested uses of said databases disclosed by Bult et al. would have motivated one of ordinary skill in the art at the time of the instant invention to use a World Wide Web resource such as KEGG for nucleotide and protein data with the clinical database directed to compounds of Antman et al. as discussed below.

73. Antman et al. discloses an improvement for "better databases" for the treatment of patients in clinical trials (page 240, Conclusions §). The database of Antman et al. comprises data directed to treatments that have no effect on mortality or are potentially harmful (page 240, Data Synthesis §) and "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) (page 246, column 1, "Negative" RCTs §). The database of Antman et al. comprises information directed to treatment therapies using a plurality of drugs

(compounds) and their effects on patients (biological systems) (page 241, column 3, lines 3 to last line), as in instant claim 17.

74. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Bult et al. for accessing resources directed to clinical type of data, and nucleotide and protein databases via the World Wide Web to access KEGG data directed to compounds and genetic data (Abstract etc.) of Ogata et al. One of ordinary skill in the art would have been motivated to build "better databases" by integrating the COMPOUND database (first database) of KEGG with the clinical type of data from compounds failed in human clinical tests as disclosed by Antman et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use KEGG wherein the COMPOUND database (first database) is directed to data from compounds failed in human clinical tests as disclosed by Ogata et al., Bult et al., and Antman et al.

75. Claims 1, 17, 59, 96, 99, and 107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goto et al. (1998) taken with Bult et al. (May 1999) in combination with Antman et al. (1992) and Wintzmann et al. (1994).

76. Goto et al. (1998), Bult et al. (May 1999), and Antman et al. (1992) disclose the limitations of claims 1, 17, 59 and 99 as discussed above.

77. However, Goto et al. (1998), Bult et al. (May 1999), and Antman et al. (1992) do not disclose the limitation of a first database comprising 2-D topological descriptors or LD50 data, as in instant claims 96 and 107.

78. Witzmann et al. discloses a method for the induction of enoyl-CoA hydratase by LD50 exposure to perfluorocarboxylic acids (compounds) and detected by 2-D electrophoresis. The inductions (effect) of peroximal enoyl-CoA hydratase and other proteins of the peroximal β-oxidative pathway (biological system) were observed following single-dose exposure to each of the plurality of compounds (Abstract etc.). The records corresponding to the chemical compounds include 2-D topological descriptors (Figure 1), as in instant claims 96 and 107.

79. Bult et al. suggests an improvement for accessing clinical type of database and nucleic and protein type of databases. Goto et al. suggests an improvement for integrating data directed to biological macromolecules such an enzymes (second database), structural information, and genetic information to better understand the functional as of biological molecules (first database) (page 591, Abstract and Introduction §). Antman et al. discloses an improvement for "better databases" directed to drug treatments (compounds) used in human clinical trials (page 240, Conclusions §). The improvements suggested by Bult et al., Goto et al., and Antman et al. are directly applicable to the data produced from Witzmann et al. via the characterization of the enoyl-CoA hydratase by LD50 exposure to perfluorocarboxylic acids (compounds) and detected by 2-D electrophoresis.

80. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Goto et al., Bult et al., and Antman et al. to integrate into the COMPOUND database (first database) of KEGG data directed to compounds effecting enoyl-CoA hydratase in the peroximal β-oxidative pathway as disclosed by Witzmann et al. Therefore, it would have been obvious to one having ordinary skill in the

art at the time of the invention was made to use the COMPOUND database of KEGG with data directed to compounds effecting enoyl-CoA hydratase in the peroximal β-oxidative pathway as disclosed by Goto et al., Bult et al., Antman et al. and Witzmann et al.

81. Claims 1, 17, 59, and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goto et al. (1998) taken with Bult et al. (May 1999) in combination with Antman et al. (1992) and Schena et al. (1996).

82. Goto et al. (1998), Bult et al. (May 1999), and Antman et al. (1992) disclose the limitations of claims 1, 17, and 59 as discussed above.

83. However, Goto et al. (1998), Bult et al. (May 1999), and Antman et al. (1992) do not disclose the limitation of a second database comprising data organized by location of expression tissues as in instant claim 126.

84. Schena et al. discloses a method for characterizing the effect of phorbol ester on enzymes (molecular targets) such as oxidases, phosphatases, and kinases (Table 2) in a biological system wherein the data (records) are organized by location of expression in tissues (page 10618, entire column 2, and Figure 3), as in claim 126.

85. Bult et al. suggests an improvement for accessing clinical type of database and nucleic and protein type of databases. Goto et al. suggests an improvement for integrating data directed to biological macromolecules such an enzymes (second database), structural information, and genetic information to better understand the functional as of biological molecules (first database) (page 591, Abstract and Introduction §). Antman et al. discloses an improvement for "better databases" directed to drug treatments (compounds) used in human

clinical trials (page 240, Conclusions §). The improvements suggested by Bult et al., Goto et al., and Antman et al. are directly applicable to the data produced from Schena et al. as directed to the characterization differential expression of genes corresponding to enzymes (molecular targets) such as oxidases, phosphatases, and kinases (Table 2) wherein the data are organized by location of expression in tissues (page 10618, entire column 2, and Figure 3).

86. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Goto et al., Bult et al., and Antman et al. to integrate the ENZYME database (second database) of KEGG with data corresponding to enzymes (molecular targets) such as oxidases, phosphatases, and kinases (Table 2) wherein the data are organized by location of expression in tissues as disclosed by Schena et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the instant invention was made to use the ENZYME database (second database) of KEGG with data corresponding to enzymes (molecular targets) such as oxidases, phosphatases, and kinases (Table 2) wherein the data are organized by location of expression in tissues as disclosed by Goto et al., Bult et al., Antman et al., and Schena et al.

CONCLUSION

87. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

(November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

88. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

89. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

90. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
5/12/04

ARDIN H. MARSCHEL
PRIMARY EXAMINER
5/14/04